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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,877	07/06/2001	Palle Schneider	10179.204-US	4404

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EXAMINER	
SLOBODYANSKY, ELIZABETH	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 02/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,877	SCHNEIDER ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky, PhD	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-34 and 36-45* is/are pending in the application.

4a) Of the above claim(s) *17,18,21-34,36-38 and 43-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16,19,20 and 39-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 16-34 and 36-45 are pending.

Election/Restrictions

Applicant's election with traverse of Group I, species at position 121, claims 16, 19, 20 and 39-42, in the reply filed on June 11, 2004 is acknowledged (Remarks, page 2, last paragraph). The traversal is on the ground(s) that "The above-captioned application was entered into the national stage under 35 U.S.C. 371. i.e. filed via the PCT. For these types of applications, the PTO follows the rules set forth in 37 C.F.R. 1.401 - 1.499. The standard for determining whether unity of invention exists during the national stage, i.e. whether a restriction requirement may be imposed, is set forth in 37 C.F.R. 1.475(a) which provides:

> An international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept.... Where a group of inventions is claimed in an application, the requirement of unity of Invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression 'special technical features' shall mean those technical features that define a contribution which each of the claimed inventions. considered as a whole, makes over the prior art."

(Remarks, page 1, emphasis added). This is not found persuasive because the instant species lack the same or corresponding special technical features for the following reasons: the shared technical feature among the species is that they are variant laccases. However, said technical feature is not a special technical feature because variant laccases are known in the prior art. The laccase variants recited in the claims have substitution at different positions, i.e. have different structures and utilities. The

recited mutations are independent form each other. Therefore, a variant laccase considered as a whole does not make a contribution over the prior art (see Office action mailed May 19, 2004, page 5).

Applicants further argue that "In the present case, the invention designated I is directed to the variants and the invention designated II is directed to methods of using the variant. Thus, the two sets of claims are related as product and a process of use of said product. Thus. under 37 C.F.R. 1.475(b)(2), the U.S. Patent and Trademark Office is required to examine these claims in a single U.S. national phase application" (Remarks, page 2). This is not persuasive because the inventions of Groups I and II lack the same or corresponding special technical features for the following reasons: variant laccases and methods of use thereof are known in the prior art and therefore, there is no special technical feature linking a variant laccase and methods of use thereof that as a whole makes a contribution over the prior art (see Office action mailed May 19, 2004, page 3). However, applicant is advised that when a product claim is found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312. In the event of rejoinder, the requirement for restriction between the product claims and the rejoined

process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

The requirement is still deemed proper and is therefore made FINAL.

Claims 17, 18, 21-34, 36-38 and 43-45 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group II, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on June 11, 2004.

Claim Objections

Claims 16 and 20 are objected to because of the following informalities: it appears that "or" is missing between "V" and "Y" in the recitation of Markush group in claim 16, line 16. It appears that "or" is missing between "R" and "S" in the recitation of Markush group in claim 20.

Appropriate correction is required.

Claim Rejections - 35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16, 19, 20 and 40-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 16, with dependent claims 19, 20 and 40-42, is drawn to a variant of a *Myceliophthora thermophila* laccase. The genus of *Myceliophthora thermophila* laccases comprises any *Myceliophthora thermophila* laccases encoded by the same or different genes. Further, different strains may have laccases with different sequences (see Applicant's Remarks filed January 12, 2004, page 7, under "Objections to the Claims").

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification the genus of *Myceliophthora thermophila* laccases is represented by the *Myceliophthora thermophila* laccase of SEQ ID NO:10. No other *Myceliophthora thermophila* laccases are disclosed in the specification. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of being a *Myceliophthora thermophila* laccase.

The specification fails to define those structural features that are commonly possessed by members of the genus that distinguish them from other members of the genus of laccases. The specification does not teach the correlation between structure

and function common to all members of said genus. Thus, one skilled in the art cannot visualize or recognize the identity of the members of the genus.

Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 16, 19, 20 and 39-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a variant of a *Myceliophthora thermophila* laccase having an amino acid sequence that differs from SEQ ID NO:10 by a mutation corresponding to at least one of the 11 specific positions therein, does not reasonably provide enablement for a variant of a *Myceliophthora thermophila* laccase having an amino acid sequence that comprises a mutation corresponding to at least one of the 11 specific positions wherein said variant amino acid sequence has an amino acid sequence at least 60% homologous with SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in

the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

It is noted that a variant laccase is required to be at least 60% homologous to SEQ ID NO:1. The term "homologous" is different from "identical". The specification discloses the GAP program used to calculate percent homology in the instant application (page 2, lines 9-13). Applicant asserts "two amino acids are homologous when they are chemically similar; they don't have to be identical. Therefore, the % homology is greater than the % identity" (Applicant's Remarks filed January 12, 2004, page 6, last paragraph). As result, SEQ ID NO:10 is about 22% identical but about 56.5% homologous to SEQ ID NO:1 (Office action mailed 8/12/03, page 3, specification on page 2, lines 30-31; Applicant's Remarks of 1/12/04, page 3). In addition, mutations are made not necessarily in SEQ ID NO:10 but in any *Myceliophthora thermophila* laccase having an unknown identity to SEQ ID NO:10. Thus, the resulting variant may have an amino acid sequence with a very low identity to SEQ ID NO:10. Taken into account that SEQ ID NO:10 is at least 20% identical to SEQ ID NO:1 and that a variant should be at least 60% homologous, i.e. roughly 20% identical, to SEQ ID NO:1, the % identity to SEQ ID NO:10 of a claimed variant should be even lower that 20%.

Claims 16, 19, 20 and 39-42 are so broad as to encompass any variant of a *Myceliophthora thermophila* laccase having an amino acid sequence comprising a mutation corresponding to at least one of the 11 specific positions in SEQ ID NO:10 with at least 60% homology to SEQ ID NO:1. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large

number of variant laccase enzymes broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of the variants having the mutations at the specific positions in SEQ ID NO:10.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any mutant *Myceliophthora thermophila* laccase having an amino acid sequence with at least 60% homology to SEQ ID NO:1 in which the amino acid(s) corresponding to the specific positions in SEQ ID NO:10 is/are mutated because the specification does **not** establish: (A) regions of the protein structure which may be

modified without effecting laccase activity; (B) the general tolerance of laccases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any laccase residues with an expectation of retaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a great number of amino acid modifications in any laccase of *Myceliophthora thermophila* sequence in addition to the specific mutations recited in the claim. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, making variant laccases is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16, 19, 20 and 39-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite the % homology. As discussed above, the percent homology can be calculated using different algorithms and parameters. Without knowing said data it is impossible to know which sequences are encompassed by the claim.

Claim 40 is unclear as reciting "protected enzyme". The specification does not define the term but states that "Protected enzymes may be prepared according to the method disclosed in EP 238,216" (page 11, lines 10-11). Thus, the metes and bounds of said term are unclear.

No art was found for the elected species of G121.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16 and 39-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Svendsen et al.

Svendsen et al. (WO 98/38286, form PTO-1449 filed July 6, 2001) teach a variant of *Myceliophthora thermophila* laccase with substitution A506E (page 7, line 14; claim 4). They teach a detergent composition comprising thereof (claims 17-20).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a variant of *Myceliophthora thermophila* laccase with substitutions at position A506 with remaining 18 amino acids. One of ordinary skill in the art would be motivated by Svendsen et al to produce a variant with different properties. One of ordinary skill in the art would have a reasonable expectation of success because

Svendsen et al teach the importance of this position. One of ordinary skill in the art would have a reasonable expectation that at least a substitution with a similar amino acids will result in similar properties.

Response to Arguments

Applicant's arguments filed January 12, 2004 in response to the Final rejection of August 12, 2003 have been fully considered but they are not persuasive.

With regard to the 112, 1st paragraph enablement rejection, Applicants argue that "The Specification describes laccases modified at specified positions. In addition, the specification provides that the variants can be modified at other positions and includes examples of such other positions. Indeed, mutations at other positions are well known in the art, See, e.g., the references relied on by the Office to reject Applicants' claims, i.e., Svendsen et al. (WO 98/38286) and Pedersen et al. (U.S. Patent No. 5.925,554). Based on Applicants' disclosure, the skilled artisan would be able to make laccase variants that are modified at the recited positions as well as other positions. Moreover, it is well known to persons of ordinary skill in the art that the amino acid sequence of enzymes from the same genus and species, e.g., *Myceliophthora thermophila,* are homologous" (Remarks, page 8). This is not persuasive because the claims are not drawn to variants comprising a limited number of specific mutations. The claims require only about 20% identity to SEQ ID NO:1, i.e. allow for changes in about 80% of the structure of SEQ ID NO:1, i.e. at about 400 positions. While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple

substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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